

Amendments to the Specification:

Replace the paragraph beginning at page 17, line 32, with the following amended paragraph:

Furthermore, an antibody of the present invention may be constructed so as to bind to a receptor that forms a hetero-dimer and changes the distance or angle between the chains or such upon ligand binding, thereby transducing signals inside the cell (for example, many cytokine receptors). The obtained antibody can be used as an agonist antibody that can ~~mimickmimic~~ the ligand-induced dimerization of a receptor.

Replace the paragraph beginning at page 24, line 7, with the following amended paragraph:

The expression vectors (pcDNA1-24H and pcDNA1-24L) for the right arm HL molecule of the antibody can be induced by tetracycline. In order to completely suppress their expression in the absence of tetracycline, the plasmid pcDNA6/TR (Invitrogen) encoding the Tet repressor (TetR) is required. TetR forms a dimer, which binds to the two Tet operator sequences (TetO2) on pcDNA4/TO and suppresses transcription of a desired gene. Once tetracycline is added, it binds to the TetR dimer and causes conformational changes, which release TetR from the Tet operator and then transcription of the desired gene is induced by the CMV/TetO2 promoter. On the other hand, the expression vectors (pIND2-7H and pIND2-7L) for the left arm HL molecule of the antibody can be induced by an analogue compound of the insect hormone ecdysone (muristerone A or ponasterone A). This system requires plasmid pVgRXR (Invitrogen) that constitutively expresses the ecdysone receptor and ~~retionid~~retinoid X receptor, which react with an ecdysone analogue compound and induce expression. Following the addition of an ecdysone analogue compound, the analogue compound, a heterodimer of ecdysone receptor, and retinoid X receptor bind to the ecdysone/glucocorticoid promoter (5XE/GRE), and activate the expression of a desired gene. Thus, a solution containing a mixture of six kinds of plasmid DNA, comprising pcDNA1-24H, pcDNA1-24L, pIND2-7H, pIND2-7L, pcDNA6/TR, and

pVgRXR, was prepared for transfection into animal cells.

Replace the paragraph beginning at page 24, line 26, with the following amended paragraph:

When COS-7 cells (Invitrogen) which are derived from the cultured cell line of African green monkey kidney were used, the cells were suspended in DMEM medium supplemented with 10% FCS, plated into each well of 6-well plates for adherent cells (CORNING) at a cell density of  $1 \times 10^5$  cells/ml, 1 ml per well, and then cultured overnight at  $37^{\circ}\text{C}$ , 5% CO<sub>2</sub> in an incubator. The plasmid solution prepared in Section 2-1 was added to a mixture of 1.5  $\mu\text{l}$  of FuGENE6 transfection reagent (Roche)(Invitrogen) and 250  $\mu\text{l}$  of Opti-MEM I medium (Invitrogen), left for 20 minutes at room temperature, and added to the cells in each well. The culture was incubated for four to five hours at  $37^{\circ}\text{C}$ , 5% CO<sub>2</sub> in an incubator.

Replace the paragraph beginning at page 25, line 8, with the following amended paragraph:

The culture medium was removed by aspiration from the cell culture transfected in Section 2-2. The culture was replenished with 1 ml of CHO-S-SFM-II (Invitrogen) containing 1  $\mu\text{g}/\text{ml}$  of tetracycline hydrochloride (WAKO Chemical), and incubated for one day at  $37^{\circ}\text{C}$ , 5% CO<sub>2</sub> in an incubator to perform the first inducible expression of the right arm HL molecule of the antibody. The culture medium was removed by aspiration, and the culture was washed once with 1 ml of CHO-S-SFM-II medium, 1 ml of the same medium containing 5  $\mu\text{M}$  of muristerone A (Invitrogen) or ponasterone A (Invitrogen) was added thereto, and incubated for two or three days at  $37^{\circ}\text{C}$ , 5% CO<sub>2</sub> in an incubator to perform the secondary induction of expression of the left arm HL molecule of the antibody, and to secrete a bispecific IgG antibody into the medium. The culture supernatant was collected, centrifuged once at about 2,000x g at room temperature for five minutes to remove the cells, and concentrated as necessary using Microcon-50 (Millipore). The sample was stored at  $4^{\circ}\text{C}$  until use.